

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte LAURA EDGERLY-PFLUG

Appeal No. 2001-1675
Application No. 08/442,077

ON BRIEF

Before WILLIAM F. SMITH, SCHEINER, and ADAMS, Administrative Patent
Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the
examiner's final rejection of claims 21-26 and 28-29, which are all the claims
pending in the application.

Claim 28 is illustrative of the subject matter on appeal and is reproduced
below:

28. A method for producing a pharmaceutical composition comprising a
liposome population having a predetermined mean particle size
comprising combination of a water-miscible organic solvent and a lipid
according to the steps of:
 - (a) preparing a first solution comprising the lipid, the solvent and an
aqueous phase and then removing the solvent so as to form
liposomes, wherein the concentration of the solvent is from about
0.5% to less than about 10% by volume of the solution;

(b) preparing a second solution comprising the lipid, the solvent and an aqueous phase and then removing the solvent so as to form liposomes, wherein the concentration of the solvent is about 10% by volume of the solution;

(c) preparing a third solution comprising the lipid, the solvent and an aqueous phase and then removing the solvent so as to form liposomes, wherein the concentration of the solvent is from about 10 to 15% by volume of the solution;

(d) determining the mean particle sizes of liposomes prepared in accordance with steps (a), (b) and (c);

(e) comparing the mean particle sizes with the solvent concentration used;

(f) selecting an organic solvent concentration corresponding to a desired mean particle size; and

(g) preparing a solution comprising the lipid, solvent and an aqueous phase, wherein the organic solvent concentration is selected according to step (f),

wherein the lipid comprises egg phosphatidylcholine and the solvent concentration in a solution is at most about 15%.

The reference relied upon by the examiner are:

Teipel	4,039,285	Aug. 2, 1977
Cambiaso et al. (Cambiaso)	4,184,849	Jan. 22, 1980
Cubicciotti et al. (Cubicciotti)	4,619,895	Oct. 28, 1986
Tenzel et al. (Tenzel)	5,000,887	Mar. 19, 1991
Leigh	EP 0 158 441	Oct. 16, 1985

GROUND OF REJECTION

Claims 21-26 and 28-29 stand rejected under 35 U.S.C. § 103 as being unpatentable over Tenzel in view of Leigh with or without Cubicciotti, Teipel or Cambiaso.

We reverse.

DISCUSSION

According to the examiner (Answer, page 4), Tenzel discloses a method of producing liposomes of uniform size. The examiner finds (id.), however, that Tenzel does not recognize the relationship between the size of the liposome and the water: solvent ratio. Therefore, the examiner relies (id.) on Leigh to teach “that the amount of water which is responsible for the hydration influences the sizes of liposomes....”

Prima facie obviousness based on a combination of references requires that the prior art provide “a reason, suggestion, or motivation to lead an inventor to combine those references.” Pro-Mold and Tool Co. v. Great Lakes Plastics Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

[E]vidence of a suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. . . . The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular.

In re Dembiczak, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) (citations omitted). The suggestion to combine prior art references must come from the cited references, not from the application’s disclosure. See In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

It is our opinion, on this record, that the examiner improperly relied on appellant’s specification to obtain the suggestion to combine Tenzel with Leigh. In this regard, the examiner finds (Answer, bridging sentence, pages 4-5), taking Tenzel and Leigh “together, it would [have] be[en] obvious to an artisan that the liposomes produced by [the] instant process will have specific uniform sizes for a

given solvent-water ratio and by changing the ratio, one can produce a population of different sized liposomes which will still be uniform in size[.]”

The examiner further relies on either the skill in the art, or the disclosure of Cubicciotti, Teipel or Cambiaso to demonstrate that the creation of a standard curve is “a routine practice in the art of chemistry.” However, none of Cubicciotti, Teipel or Cambiaso disclose liposomes, let alone “teach or suggest [a] liposome preparation at organic solvent concentrations of about 15% or less, or varying organic solvent concentration so as to achieve a desired mean liposome size” as is required by the claimed invention. Reply Brief, page 2. In addition, both Tenzel and Leigh teach liposome preparation at organic solvent concentrations “higher than the maximum employed in applicant’s claimed method.” Brief, page 3; see also, Reply Brief, page 2.

We note the examiner’s explanation of the general principle relating to “compound-solvent interactions”, concluding (Answer, page 6) that “if too much [] solvent is present, the composition becomes a dilute solution of the membrane lipid in organic solvent...” The examiner, however, simply does not identify where the claimed limitation -- of a solvent concentration that is at most about 15% -- is taught by the combination of references relied upon.

As set forth in In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000):

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field.... Close adherence to this methodology is especially important in cases where the very ease with which the invention

can be understood may prompt one “to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher.”

...
Most if not all inventions arise from a combination of old elements. ... Thus, every element of a claimed invention may often be found in the prior art.... However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention.... Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. [citations omitted]

In other words, “there still must be evidence that ‘a skilled artisan, ... with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.’” Ecolochem Inc. v. Southern California Edison, 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1075-76 (Fed. Cir. 2000). On the record before us, we find no reasonable suggestion for combining the teachings of the references relied upon by the examiner in a manner which would have led one of ordinary skill in this art to arrive at the claimed invention. Therefore, it is our opinion that the examiner has failed to meet his burden¹ of providing the evidence necessary to support a prima facie case of obviousness.

¹ The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

Accordingly, we reverse the rejection of claims 21-26 and 28-29 under 35 U.S.C. § 103 as being unpatentable over Tenzel in view of Leigh with or without Cubicciotti, Teipel or Cambiaso.

REVERSED

William F. Smith)	
Administrative Patent Judge)	
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)	
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